AMENDMENTS TO THE CLAIMS:

Please amend claims 4, 18, 65 and 69 as follows. This listing of claims replaces all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1. (Previously presented) A substantially purified single or two chain MTSP7 polypeptide-or a catalytically active portion of the polypeptide, wherein the polypeptide is selected from the group consisting of:

a) a polypeptide that comprises a sequence of amino acids having at least about 90% amino acid sequence identity with the sequence of amino acids set forth in SEQ ID No. 16; and

b) a polypeptide that comprises a sequence of amino acids encoded by the sequence of nucleotides set forth in SEQ ID No. 15; and

the polypeptide has serine protease activity.

2. (Previously presented) The polypeptide of claim 1 that is an activated two chain polypeptide.

3. (Cancelled)

4. (Currently amended) A substantially purified single or two chain polypeptide, comprising an MTSP7 portion, wherein:

said [[the]] MTSP7 portion is the only MTSP7 portion of the single or two chain polypeptide ~~consists essentially of~~ and is a [[the]] protease domain of [[the]] MTSP7 ~~or a catalytically active portion thereof~~;

~~the protease domain of the MTSP7 or the catalytically active portion thereof is~~ selected from the group consisting of

a) a polypeptide consisting essentially of the sequence of amino acids encoded by the sequence of nucleotides set forth in SEQ ID No. 17; [[and]]

b) a polypeptide consisting essentially of the sequence of amino acids that has at least about 90% amino acid sequence identity with the sequence of amino acids set forth as SEQ ID No. 18; and

c) a polypeptide that is a catalytically active portion of a) or b);

and the MTSP7 portion of the polypeptide has serine protease activity.

5. (Original) The substantially purified polypeptide of claim 1, wherein the MTSP7 is a human polypeptide.

6. (Previously presented) The substantially purified polypeptide of claim 4 that comprises an N terminal cleavage site or activated cleavage site and a catalytic triad of His, Asp and Ser residues.

7. (Cancelled)

8. (Original) The substantially purified polypeptide of claim 1 that comprises the sequence of amino acids set forth in SEQ ID No. 16.

9. (Original) The substantially purified polypeptide of claim 1 that comprises the sequence of amino acids set forth in SEQ ID No. 18.

10. (Original) The substantially purified polypeptide of claim 1, wherein the protease domain comprises the sequence of amino acids set forth as amino acids 206-438 of SEQ ID No. 16.

11.-17. (Cancelled)

18. (Currently amended) The polypeptide of claim [[15]] 1, wherein a free Cysteine in the protease domain is replaced with another amino acid.

19. (Original) The polypeptide of claim 18, wherein the replacing amino acid is a serine.

20. – 49. (Cancelled)

50. (Original) A conjugate, comprising:

a polypeptide of claim 1, and

a targeting agent linked to the polypeptide directly or via a linker.

51. (Original) The conjugate of claim 50, wherein the targeting agent permits

affinity isolation or purification of the conjugate;

attachment of the conjugate to a surface;

detection of the conjugate; or

targeted delivery to a selected tissue or cell.

52. (previously presented) A conjugate, comprising:

a polypeptide of claim 4; and

a targeting agent linked to the polypeptide directly or via a linker.

53. (Original) The conjugate of claim 52, wherein the targeting agent permits

affinity isolation or purification of the conjugate;

attachment of the conjugate to a surface;

detection of the conjugate; or

targeted delivery to a selected tissue or cell.

54. (Original) A conjugate, comprising:

a polypeptide of claim 6; and

a targeting agent linked to the polypeptide directly or via a linker.

55. (Original) The conjugate of claim 54, wherein the targeting agent permits

affinity isolation or purification of the conjugate;

attachment of the conjugate to a surface;

detection of the conjugate; or

targeted delivery to a selected tissue or cell.

56. – 58. (Cancelled)

59. (Original) A solid support comprising two or more polypeptides of claim 1 linked thereto either directly or via a linker.

60. (Original) The support of claim 59, wherein the polypeptides comprise an array.

61. (Original) The support of claim 59, wherein the polypeptides comprise a plurality of different protease domains.

62. – 64. (Cancelled)

65. (currently amended) A method for identifying compounds that modulate the protease activity of a polypeptide, comprising:

contacting a polypeptide of claim 1 with a substrate that is proteolytically cleaved by the polypeptide, and, either simultaneously, before or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and

selecting compounds that change the amount of substrate cleaved compared to a control, whereby compounds that modulate the activity of the polypeptide are identified and the identified compounds inhibit tumorigenesis.

66. (Original) The method of claim 65, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof that modulate the activity of the polypeptide.

67. (Original) The method of claim 65, wherein a plurality of the test substances are screened simultaneously.

68. (Cancelled)

69. (currently amended) A method for identifying compounds that modulate the protease activity of a polypeptide, comprising:

contacting a polypeptide of claim 4 with a substrate that is proteolytically cleaved by the polypeptide, and, either simultaneously, before or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and

selecting compounds that change the amount of substrate cleaved compared to a control, whereby compounds that modulate the activity of the polypeptide are identified and the identified compounds inhibit tumorigenesis.

70. (Original) The method of claim 65, wherein the change in the amount of substrate cleaved is assessed by comparing the amount of substrate cleaved in the presence of the test compound with the amount of substrate cleaved in the absence of the test compound.

71. (Original) The method of claim 67, wherein a plurality of the polypeptides are linked to a solid support, either directly or via a linker.

72. (Original) The method of claim 71, wherein the polypeptides comprise an array.

73. (Withdrawn) A method of identifying a compound that specifically binds to a single-chain and/or two-chain protease domain and/or to single or two-chain full length polypeptide, comprising:

contacting a polypeptide of claim 1 with a test compound or plurality thereof under conditions conducive to binding thereof; and

identifying compounds that specifically bind to the polypeptide single chain protease domain, or two chain form thereof, the full length or two chain form of the full length polypeptide or compounds that inhibit binding of a compound known to bind to the polypeptide single chain protease domain or two chain form thereof or the two chain form of

the full length polypeptide, wherein the known compound is contacted with the polypeptide before, simultaneously with or after the test compound.

74. (Withdrawn) The method of claim 73, wherein the polypeptide is linked either directly or indirectly via a linker to a solid support.

75. (Withdrawn) The method of claim 73, wherein the test compounds are small molecules, peptides, peptidomimetics, natural products, antibodies or fragments thereof.

76. (Withdrawn) The method of claim 73, wherein a plurality of the test substances are screened simultaneously.

77. (Withdrawn) The method of claim 73, wherein a plurality of the polypeptides are linked to a solid support.

78. (Withdrawn) A method of identifying a compound that specifically binds to a single-chain and/or two-chain protease domain and/or to single or two-chain full length polypeptide, comprising:

contacting a polypeptide of claim 4 with a test compound or plurality thereof under conditions conducive to binding thereof; and

identifying compounds that specifically bind to the polypeptide single chain protease domain, or two chain form thereof, the full length or two chain form of the full length polypeptide or compounds that inhibit binding of a compound known to bind to the polypeptide single chain protease domain or two chain form thereof or the two chain form of the full length polypeptide, wherein the known compound is contacted with the polypeptide before, simultaneously with or after the test compound.

79. (Withdrawn) A method for identifying activators of the zymogen form of an MTSP7, comprising:

contacting a zymogen form of the polypeptide of claim 1 with a substrate of the activated form of the polypeptide;

adding a test compound, wherein the test compound is added before, after or simultaneously with the addition of the substrate; and

detecting cleavage of the substrate, thereby identifying compounds that activate the zymogen.

80. (Withdrawn) The method of claim 79, wherein the substrate is a chromogenic substrate.

81. (Withdrawn) The method of claim 79, wherein the substrate is a L-pyroglutamyl-L-prolyl-L-arginine-p-nitroaniline hydrochloride.

82. (Withdrawn) The method of claim 79, wherein the test compound is a small molecule, a nucleic acid or a polypeptide.

83. (Withdrawn) A method for treating or preventing a neoplastic disease, in a mammal, comprising administering to a mammal an effective amount of an inhibitor of a polypeptide of claim 1.

84. (Withdrawn) The method of claim 83, wherein the inhibitor is an antibody that specifically binds to the polypeptide, or a fragment or derivative of the antibody containing a binding domain thereof, wherein the antibody is a polyclonal antibody or a monoclonal antibody.

85. (Withdrawn) A method for treating or preventing a neoplastic disease, in a mammal, comprising administering to a mammal an effective amount of an inhibitor of a polypeptide of claim [[3]] 4.

86. (Withdrawn) A method for treating or preventing a neoplastic disease, in a mammal, comprising administering to a mammal an effective amount of an inhibitor of a polypeptide of claim 6.

87. (Withdrawn) A method of inhibiting tumor initiation, growth or progression or treating a malignant or pre-malignant condition, comprising administering an agent that inhibits activation cleavage of the zymogen form of a polypeptide of claim 1 or an activity of the activated form.

88. (Withdrawn) The method of claim 87, wherein the condition is a condition of the breast, cervix, prostate, lung, ovary or colon.

89. (Withdrawn) The method of claim 87, wherein the agent is an antisense oligonucleotide, double-stranded RNA (dsRNA) or an antibody.

90. (Withdrawn) The method of claim 87, further comprising administering another treatment or agent selected from anti-tumor and anti-angiogenic treatments or agents.

91. (Withdrawn) A method of inhibiting tumor initiation, growth or progression or treating a malignant or pre-malignant condition, comprising administering an agent that inhibits activation cleavage of the zymogen form of a polypeptide of claim 4 or an activity of the activated form.

92. (Withdrawn) The method of claim 91, wherein the condition is a condition of the breast, cervix, prostate, lung, ovary or colon.

93. (Withdrawn) The method of claim 91, wherein the agent is an antisense oligonucleotide, double-stranded RNA (dsRNA) or an antibody.

94. (Withdrawn) The method of claim 91, further comprising administering another treatment or agent selected from anti-tumor and anti-angiogenic treatments or agents.

95. (Withdrawn) A method of identifying a compound that binds to the single-chain and/or two-chain form of a polypeptide of claim 1, comprising:

contacting a test compound with both forms;

determining to which form the compound binds; and

if it binds to a form of polypeptide, further determining whether the compound has at least one of the following properties:

(i) inhibits activation cleavage of the single-chain zymogen form of polypeptide;

(ii) inhibits activity of the two-chain or single-chain form; and

(iii) inhibits dimerization of the polypeptide.

96. (Withdrawn) The method of claim 95, wherein both forms consist essentially of the protease domain produced by cleavage between the arginine and isoleucine in either the single- or two-chain form.

97. (Withdrawn) A method of identifying a compound that binds to the single-chain and/or two-chain form of a polypeptide of claim 4, comprising:

contacting a test compound with both forms;

determining to which form the compound binds; and

if it binds to a form of polypeptide, further determining whether the compound has at least one of the following properties:

(i) inhibits activation cleavage of the single-chain zymogen form of polypeptide;

(ii) inhibits activity of the two-chain or single-chain form; and

(iii) inhibits dimerization of the polypeptide.

98. (Withdrawn) The method of claim 97, wherein both forms consist essentially of the protease domain produced by cleavage between the R and I in either the single- or two-chain form.

99. (Withdrawn) A method of detecting neoplastic disease, comprising: detecting a polypeptide that comprises a polypeptide of claim 1 in a biological sample, wherein the amount detected differs from the amount of polypeptide detected from a subject who does not have neoplastic disease.

100. (Withdrawn) The method of claim 99, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial fluid, sweat, interstitial fluid, sperm, cerebrospinal fluid, ascites fluid, tumor tissue biopsy and circulating tumor cells.

101. (Withdrawn) A method of detecting neoplastic disease, comprising: detecting a polypeptide that comprises a polypeptide of claim 4 in a biological sample, wherein the amount detected differs from the amount of polypeptide detected from a subject who does not have neoplastic disease.

102. (Withdrawn) The method of claim 101, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial fluid, sweat, interstitial fluid, sperm, cerebrospinal fluid, ascites fluid, tumor tissue biopsy and circulating tumor cells.

103. (Withdrawn) A method of detecting neoplastic disease, comprising: detecting a polypeptide that comprises a polypeptide of claim 6 in a biological sample, wherein the amount detected differs from the amount of polypeptide detected from a subject who does not have neoplastic disease.

104. (Withdrawn) The method of claim 103, wherein the biological sample is selected from the group consisting of blood, urine, saliva, tears, synovial fluid, sweat, interstitial fluid, sperm, cerebrospinal fluid, ascites fluid, tumor tissue biopsy and circulating tumor cells.

105. (Withdrawn) A method of diagnosing the presence of a pre-malignant lesion, a malignancy, or other pathologic condition in a subject, comprising:

obtaining a biological sample from the subject; and

exposing it to a detectable agent that binds to a two-chain and/or single-chain form of a polypeptide of claim 1, wherein the pathological condition is characterized by the presence or absence of the two-chain or single-chain form.

106. (Withdrawn) A method of diagnosing the presence of a pre-malignant lesion, a malignancy, or other pathologic condition in a subject, comprising:

obtaining a biological sample from the subject; and

exposing it to a detectable agent that binds to a two-chain and/or single-chain form of a polypeptide of claim 4, wherein the pathological condition is characterized by the presence or absence of the two-chain or single-chain form.

107. (Withdrawn) A method of diagnosing the presence of a pre-malignant lesion, a malignancy, or other pathologic condition in a subject, comprising:

obtaining a biological sample from the subject; and

exposing it to a detectable agent that binds to a two-chain and/or single-chain form of a polypeptide of claim 6, wherein the pathological condition is characterized by the presence or absence of the two-chain or single-chain form.

108. (Withdrawn) A method of monitoring tumor progress and/or therapeutic effectiveness, comprising detecting and/or quantifying the level of a polypeptide of claim 1 in a body tissue or fluid sample.

109. (Withdrawn) The method of claim 108, wherein the tumor is a tumor of the breast, cervix, prostate, lung, ovary or colon.

110. (Withdrawn) The method of claim 108, wherein the body fluid is blood, urine, sweat, saliva, cerebrospinal fluid and synovial fluid.

111. (Withdrawn) A method of monitoring tumor progress and/or therapeutic effectiveness, comprising detecting and/or quantifying the level of a polypeptide of claim 4 in a body tissue or fluid sample.

112. (Withdrawn) The method of claim 111, wherein the tumor is a tumor of the breast, cervix, prostate, lung, ovary or colon.

113. (Withdrawn) The method of claim 111, wherein the body fluid is blood, urine, sweat, saliva, cerebrospinal fluid and synovial fluid.

114. (Withdrawn) A method of monitoring tumor progress and/or therapeutic effectiveness, comprising detecting and/or quantifying the level of a polypeptide of claim 6 in a body tissue or fluid sample.

115. (Withdrawn) The method of claim 114, wherein the tumor is a tumor of the breast, cervix, prostate, lung, ovary or colon.

116. (Withdrawn) The method of claim 114, wherein the body fluid is blood, urine, sweat, saliva, cerebrospinal fluid and synovial fluid.

117. (Previously presented) The polypeptide of claim 4, wherein a free Cysteine in the protease domain is replaced with another amino acid.

118. (Previously presented) The polypeptide of claim 117, wherein the replacing amino acid is a serine.

119. (Previously presented) A substantially purified activated two chain polypeptide, comprising the protease domain of a type-II membrane-type serine protease 7 (MTSP7) or a catalytically active portion thereof, wherein the polypeptide has at least about 90% amino acid sequence identity with the sequence of amino acids set forth in SEQ ID No. 16; and the polypeptide has serine protease activity.

120. (Previously presented) A substantially purified activated two chain polypeptide, comprising the protease domain of a type-II membrane-type serine protease 7 (MTSP7) or a catalytically active portion thereof, wherein the protease domain or catalytically active portion thereof has at least about 90% amino acid sequence identity with the sequence of amino acids set forth in SEQ ID No. 18; and the polypeptide has serine protease activity.

121. (Previously presented) A substantially purified single or two chain polypeptide, comprising the protease domain of a type-II membrane-type serine protease 7 (MTSP7) or a catalytically active portion thereof, wherein the polypeptide has at least about 80% amino acid sequence identity with the sequence of amino acids set forth in SEQ ID No. 16; and the polypeptide has serine protease activity.

122. (Previously presented) A substantially purified single or two chain polypeptide consisting essentially of the protease domain of a type-II membrane-type serine protease 7 (MTSP7) or a catalytically active portion thereof, wherein the protease domain or catalytically active portion thereof has at least about 80% amino acid sequence identity with the sequence of amino acids set forth in SEQ ID No. 18; and the polypeptide has serine protease activity.